

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
2 June 2005 (02.06.2005)

PCT

(10) International Publication Number
WO 2005/049600 A1

(51) International Patent Classification⁷: C07D 401/04,
A61P 25/00, A61K 31/4439

(21) International Application Number:
PCT/EP2004/012772

(22) International Filing Date:
10 November 2004 (10.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0326407.4 12 November 2003 (12.11.2003) GB

(71) Applicant (for all designated States except US): **GLAXO
GROUP LIMITED** [GB/GB]; Glaxo Wellcome House,
Berkeley Avenue, Greenford Middlesex UB6 0NN (GB).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **ALVARO, Giuseppe**

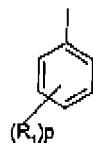
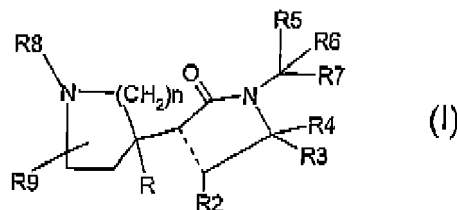
[IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **DI FABIO, Romano** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **GIOVANNINI, Riccardo** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **PAIO, Alfredo** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **TRANQUILLINI, Maria, Elvira** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT). **MATTIOLI, Lucia** [IT/IT]; GlaxoSmithKline, Via Alessandro Fleming 2, I-37100 Verona (IT).

(74) Agent: **GIDDINGS, Peter, John**; GlaxoSmithKline, 980 Great West Road (CN925.1), Brentford, Middlesex TW8 9GS (GB).

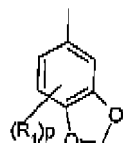
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

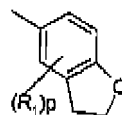
(54) Title: **BETA-LACTAMS FOR TREATMENT OF CNS DISORDERS**



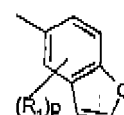
(i)



(ii)



(iii)



(iv)

(57) Abstract: The present invention relates to novel compounds of formula (I) wherein ---- represents a single or a double bond; R represents a radical selected from formulae i), ii), iii) and iv) in which R₁ is halogen, cyano, C₁₋₄ alkyl, C₁₋₄ alkoxy, trifluoromethyl or trifluoromethoxy and p is zero or an integer from 1 to 3; R₂ represents hydrogen or C₁₋₄ alkyl; R₃ represents hydrogen, hydroxy or C₁₋₄ alkyl; R₄ represents hydrogen or R₄ together with R₃ represents =O or =CH₂; R₅ represents phenyl, naphthyl, a 9 to 10 membered fused bicyclic heterocyclic group or a 5 or 6 membered heteroaryl group, wherein said groups are optionally substituted by 1 to 3 groups independently selected from trifluoromethyl, C₁₋₄ alkyl, hydroxy, cyano, C₁₋₄ alkoxy, trifluoromethoxy, halogen or S(O)_qC₁₋₄ alkyl; R₆ and R₇ independently represent hydrogen, cyano, C₁₋₄ alkyl; R₈ is (CH₂)_rR₁₀; R₉ represents hydrogen, halogen, C₃₋₇ cycloalkyl, hydroxy, nitro, cyano or C₁₋₄ alkyl optionally substituted by one or two groups selected from halogen, cyano, hydroxy or C₁₋₄ alkoxy; R₁₀ represents hydrogen or C₃₋₇ cycloalkyl; n represents 1 or 2; q is 0, 1 or 2; r is 0 or an integer from 1 to 4; or a pharmaceutically acceptable salt or a solvate thereof, process for their preparation and their use in the treatment of conditions mediated by tachykinins and/or by selective inhibition of the serotonin reuptake transporter protein.